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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/598,703	09/08/2006	Vasilis Ntziachristos	MGH-048AUS	9134

22494 7590 01/04/2010
DALY, CROWLEY, MOFFORD & DURKEE, LLP
SUITE 301A
354A TURNPIKE STREET
CANTON, MA 02021-2714

EXAMINER

BAKER, DAVID S

ART UNIT	PAPER NUMBER
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2884

NOTIFICATION DATE	DELIVERY MODE
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01/04/2010

ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No. 10/598,703	Applicant(s) NTZIACHRISTOS ET AL.	
	Examiner David S. Baker	Art Unit 2884	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 15 October 2009.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-41, 44, 45, 47 and 49-51 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-6, 8-27, 29-41, 44, 45, 47 and 49-51 is/are rejected.
- 7) ☒ Claim(s) 7 and 28 is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
 2. ☐ Certified copies of the priority documents have been received in Application No. _____.
 3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413)
Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftperson's Patent Drawing Review (PTO-948) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)
Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 15 October 2009 has been entered.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

3. Claim 40 is rejected under 35 U.S.C. 102(b) as being anticipated by Seibel (US 2001/0055462 A1).

Regarding claim 40, Seibel discloses a scanning optical system, comprising: at least one selectively movable component to selectively move a projection direction of an apparent light source to direct a plurality of light paths toward a specimen (F:3a-3b; P:000077-0078), wherein the at least one selectively movable component includes a selectively movable structure comprising an optical fiber (F:3a-3b; P:000077-0078), wherein the selectively movable structure is configured to move the optical fiber to a plurality of physical locations to provide the plurality of light paths (F:3a-3b; P:000077-0078).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 1-6, 9-11, 13, 19-26, 29-30, 32, 38-39, 44-45, 47, and 49-51 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ntziachristos (WO 2002/041760 A2) in view of Seville (US 2002/0089658 A1) and Freeman (US 2003/0124244 A1).

Regarding claims 1 and 21, Ntziachristos discloses a system and method for optical tomography comprising: generating an excitation light with an apparent light source adapted to project the excitation light toward a specimen (P:3 L:11-22) having fluorescent proteins therein (P:13 L:5-18); wherein the excitation light enters the specimen becoming intrinsic light within the specimen (P:18 L:15-31); wherein the intrinsic light is adapted to excite fluorescent light from fluorochromes (P:18 L:15-31), and the wherein intrinsic light and the emitted light have wavelengths in the visible

wavelength region, the visible wavelength range spanning from about 400 nanometers to about 700 nanometers (C:3 L:43-54); a light detector configured to receive intrinsic light exiting the specimen and configured to receive fluorescent light exiting the specimen (P:37 L:8-19); and a processor for receiving the image signal (F:24). Ntziachristos does not explicitly disclose that the fluorechrome is a protein or an image processor coupled to the light detector and configured to use a light propagation model, wherein the light propagation model is configured to predict propagation of visible light in a diffuse medium, wherein the image processor comprises a diffusion equation processor configured to use a diffusion equation having a modified diffusion coefficient selected in accordance with the propagation of visible light in the diffuse medium throughout a substantial portion of the visible wavelength region. Seville discloses a method of fluorescence detection involving the impingement of visible wavelength light (abstract) upon fluorescent proteins within a sample (abstract). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to utilize the teaching of Seville to modify the system of Ntziachristos to use fluorescent proteins rather than fluorochromes with protein transport mediators. The motivation for doing so would have been to reduce the complexity of the dyeing process by eliminating the mediator component; Seville teaches using the protein as the fluorochrome itself. Doing so would reduce preparation time in the dyeing process. Freeman discloses an image method configured to use a light propagation model (P:0019, 0030-0043), wherein the light propagation model is configured to predict propagation of visible light in a diffuse medium (P:0019, 0030-0043), wherein the method is configured to use a diffusion

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equation having a modified diffusion coefficient selected in accordance with the propagation of visible light in the diffuse medium throughout a substantial portion of the visible wavelength region (F:3-4; P:0019, 0030-0043). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to program the processor of Ntziachristos to perform such diffusion modeling as taught by Freeman. The motivation for doing so would have been to improve the image quality of the resultant datasets.

Regarding claims 2 and 22, Ntziachristos discloses that the intrinsic and fluorescent lights are diffuse (P:3 L:23 thru P:4 L:6).

Regarding claims 3 and 23, Ntziachristos discloses that the fluorescent emission light of the fluorochrome Cy 5.5 is 694nm (P:18 L:15-31).

Regarding claims 4 and 24, Ntziachristos discloses that the fluorescent emission light of the fluorochrome Cy 5.5 is 694nm (P:18 L:15-31).

Regarding claims 5 and 25, Ntziachristos discloses that the fluorescent emission light of the fluorochrome ICG is 800nm (P:18 L:15-31).

Regarding claims 6 and 26, Ntziachristos discloses that the light detector is further configured for converting the received intrinsic light into first image information (P:3 L:23 thru P:4 L:6); further configured for converting the received fluorescent light into second image information (P:3 L:23 thru P:4 L:6); and wherein the image processor further combines the first image information, the second image information, and the light propagation model (P:15 L:15 thru P:16 L:25); and further provides a tomographic image of the fluorescent fluorochromes/proteins (P:15 L:15 thru P:16 L:25).

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Regarding claim 9, Ntziachristos discloses an optical scanner to provide the intrinsic light and fluorescent light to the light detector on a plurality of light paths relative to the specimen (F:2a, F:3a-3f; P:21 L:9-30).

Regarding claims 10 and 29, Ntziachristos discloses that the apparent light source is selectively moved by a light directing device to direct the excitation light on a plurality of light paths toward the specimen (P:18 L:22 thru P:19 L:19).

Regarding claims 11 and 30, Ntziachristos discloses an optical switch selectively moves the apparent light source to provide a plurality of light paths toward the specimen (P:18 L:22 thru P:19 L:19).

Regarding claims 13 and 32, Ntziachristos discloses that the apparent light source is selectively moved by a light directing device to direct the excitation light in translation along a translation axis (F:3a-3f; P:21 L:9-22).

Regarding claims 19 and 38, Ntziachristos discloses that the intrinsic light passes through the specimen as transillumination light (P:2 L:3-13, P:3 L:11-27).

Regarding claims 20 and 39, Ntziachristos discloses that the intrinsic light reflects from the specimen as reflectance light (P:21 L:9-22).

Regarding claims 44-45, Ntziachristos discloses that the intrinsic light or emitted light propagates through the specimen a distance greater than 0.5mm (P:1 L:20 thru P:2 L:13, P:3 L:11-22).

Regarding claims 47 and 49, Ntziachristos discloses that the intrinsic light has a wavelength, 694nm, in the visible wavelength range and outside the NIR range (C:3 L:43-54).

Regarding claim 50 and 51, Ntziachristos, Seville and Freeman do not explicitly disclose that the modified diffusion coefficient is selected in accordance with the propagation of visible light in the diffusion medium down to 400nm. However, Freeman discloses that when solving the diffusion equation, appropriate boundary conditions must be taken into consideration (P:0032). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to select the appropriate boundary condition such that the diffusion coefficient correctly anticipates the propagation of visible light in the wavelength range, down to 400nm, desired. The motivation for doing so would have been to increase the precision of the device by allowing for the correct model of all data in a set collected thereby resulting in a more robust image.

7. Claims 8, 12, 14-18, 27, 31, and 33-37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Ntziachristos (WO 2002/041760 A2), Seville (US 2002/0089658 A1), Freeman (US 2003/0124244 A1), and further in view of Takada (EP 0336208 A1).

Regarding claims 8 and 27, Ntziachristos, Seville and Freeman do not explicitly disclose a selectively movable detector. Ntziachristos discloses that the projection direction of the apparent light source is selectively moved by a light directing device to move the excitation light on a plurality of light paths toward the specimen (P:18 L:22 thru P:19 L:19). Takada discloses a fluorescent computed tomography system and method comprising: a selectively movable stage upon which the specimen is located and selectively moved that provides the excitation light on a plurality of light paths relative to the specimen (F:1; C:4 L:6-47). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to provide a movable stage as taught by

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Takada in combination with the selectively movable apparent light source of Ntziachristos. The motivation for doing so would have been to improve the physical range over which the specimen may be examined. The movement between the light source and the specimen versus that of the detector is a matter of apparent motion in different frames of reference. It would be a simple matter of design choice for one of ordinary skill in the art at the time the invention was made to employ a selectively movable light source, specimen, detector, or any combination thereof.

Regarding claims 12 and 31, Ntziachristos, Seville and Freeman do not explicitly disclose a selectively movable mirror. Takada discloses a fluorescent computed tomography system and method comprising: a selectively movable mirror that moves the projection direction of the apparent light source to provide a plurality of light paths toward the specimen (F:1; C:3 L:50 thru C:4 L:5). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to utilize the movable mirror of Takada as a light diverting means in the apparatus of Ntziachristos. The motivation for doing so would have been to decrease the cost of the light diversion set up since by using a simple mirror rather than an optical switch with several optical fibers.

Regarding claims 14 and 33, Ntziachristos, Seville and Freeman do not explicitly disclose that the specimen is selectively movable to provide the excitation light on a plurality of light paths relative to the specimen. Takada discloses a fluorescent computed tomography system and method comprising: a selectively movable stage upon which the specimen is located and selectively moved that provides the excitation light on a plurality of light paths relative to the specimen (F:1; C:4 L:6-47). At the time the invention was

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made, it would have been obvious to a person of ordinary skill in the art to provide a movable stage as taught by Takada as the specimen holder of Ntziachristos. The motivation for doing so would have been to improve the physical range over which the specimen may be examined.

Regarding claims 15 and 34, Ntziachristos, Seville, Freeman, and Takada do not explicitly disclose that the specimen is selectively movable in a rotation about a specimen rotation axis. However, at the time the invention was made, it would have been obvious to a person of ordinary skill in the art to alter the specimen stage of Ntziachristos and Takada to allow for rotation. The motivation for doing so would have been to improve the physical range over which the specimen may be examined.

Regarding claims 16 and 35, Takada disclose that the specimen is selectively movable in translation along at least one specimen translation axis (F:1; C:4 L:6-47).

Regarding claims 17 and 36, Takada disclose that the specimen is selectively movable in translation along at least one specimen translation axis (F:1; C:4 L:6-47), but Ntziachristos, Seville, Freeman, and Takada do not explicitly disclose that the specimen is selectively movable in a rotation about a specimen rotation axis. However, at the time the invention was made, it would have been obvious to a person of ordinary skill in the art to alter the specimen stage of Ntziachristos and Takada to allow for rotation. The motivation for doing so would have been to improve the physical range over which the specimen may be examined.

Regarding claims 18 and 37, Ntziachristos discloses that the projection direction of the apparent light source is selectively moved by a light directing device to move the

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excitation light on a plurality of light paths toward the specimen (P:18 L:22 thru P:19 L:19). Ntziachristos does not disclose expressly that the specimen is selectively movable to provide the excitation light on a plurality of light paths relative to the specimen.

Takada discloses a fluorescent computed tomography system and method comprising: a selectively movable stage upon which the specimen is located and selectively moved that provides the excitation light on a plurality of light paths relative to the specimen (F:1; C:4 L:6-47). At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to provide a movable stage as taught by Takada as the specimen holder of Ntziachristos. The motivation for doing so would have been to improve the physical range over which the specimen may be examined.

8. Claim 41 is rejected under 35 U.S.C. 103(a) as being unpatentable over Seibel (US 2001/0055462 A1).

Regarding claim 41, the examiner takes Official Notice that movable mirrors are well known in the art of scanning imagery. At the time the invention was made, it would have been obvious to a person of ordinary skill in the art to use movable mirror in the system of Seibel. The motivation for using such a device would have been to better focus the excitation light into the optical fiber.

Allowable Subject Matter

9. Claims 7 and 28 are objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.
10. The following is a statement of reasons for the indication of allowable subject matter:

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Regarding claim 7, the prior art of record fails to disclose or reasonably suggest, along with the other claimed limitations, a system for optical tomography comprising, namely: wherein the modified diffusion coefficient has the claimed form.

Regarding claim 28, the prior art of record fails to disclose or reasonably suggest, along with the other claimed limitations, a method of optical tomography comprising, namely: wherein the modified diffusion coefficient has the claimed form.

Response to Arguments

11. Applicant's arguments, see pages 11-13 of the amendment, filed 15 October 2009, with respect to the rejections of claims 46 and 48 have been fully considered and are persuasive. The rejections of said claims under 35 U.S.C. 112, second paragraph have been withdrawn.

12. Applicant's arguments filed 15 October 2009 have been fully considered but they are not persuasive.

The applicant alleges that Ntziachristos fails to disclose the use of intrinsic light within the visible wavelength range of about 400-700nm; the examiner respectfully disagrees. Ntziachristos discloses at least the use of light from about 550-700nm (C:3 L:43-54).

The applicant alleges that the examiner's conclusion as to the obviousness of a selectively movable detector is impermissible; the examiner respectfully disagrees. In so far as the selectively movable detector is only used to scan the specimen and receive the intrinsic and fluorescent light, the examiner maintains such a limitation would have been obvious to a person of ordinary skill in the art at the time the invention was made. Absent some new or unexpected result, the examiner cannot see how the use of a movable detector in place of a movable apparent light source would result in different data collected. As such, the applicant's arguments are not

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persuasive. The examiner also reminds the applicant that it is obvious to try such a solution since the movement of the light source is essentially a choice from a number of finite predictable solutions. If a specimen is to be scanned either the light source must move, the specimen must move, or the detector must move. When there are a finite number of identified, predictable solutions, a person of ordinary skill in the art has good reason to pursue the known options within his or her technical grasp. *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1397 (U.S. 2007)

13. Applicant's arguments with respect to claims 1, 21, 40, and their dependants have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

14. Any inquiry concerning this communication or earlier communications from the examiner should be directed to David S. Baker whose telephone number is (571) 272-6003. The examiner can normally be reached on MTWRF 12:00p - 8:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, David P. Porta can be reached on (571) 272-2444. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/David P. Porta/
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2884

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